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A Case of Pituitary Adenoma Associated with McCune-Albright Syndrome

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Abstract. **A 11-year-old boy presented with right temporal hemianopsia and was evaluated of a possible pituitary adenoma. At the age of six, he underwent surgery for facial deformities due to fibrous dysplasia. On admission, he had acromegalic features, was 170 cm tall, weighing 66 kg. The left side of his face was slightly deformed, and a café-au-lait spot was found on his right face. Endocrinologic examination revealed elevated basal level of serum GH (103.6 ng/ml, normal <3 ng/ml) and PRL (259.1 ng/ml, normal <30 ng/ml). Other endocrine functions were normal. CT showed hyperostosis of the right frontal, occipital, sphenoidal and maxillary bones. Magnetic resonance imaging (MRI) revealed a pituitary macroadenoma with intraadenomatous cyst. On the basis of physical, endocrinologic and neuroradiologic examination, our diagnosis was pituitary adenoma with McCune-Albright syndrome. Surgery was performed by subfrontal approach. By light microscopy, the pituitary tumor represented a typical acidophilic adenoma. Immunoreactivity for GH and PRL were evident in most of the adenoma cells. Double immunostaining for GH and PRL demonstrated the co-existence of the two hormones in a few adenoma cells. However the majority of cells expressed only one hormone. After surgery the right temporal hemianopsia improved. Postsurgical endocrinologic examination revealed reduction in basal serum GH and PRL levels. Administration of bromocriptine decreased blood PRL levels but it had a limited action on GH hypersecretion.**

Keywords. **pituitary, McCune-Albright syndrome, pathology**

Introduction

McCune-Albright syndrome comprises a triad of: localized bone lesions termed polyostotic fibrous dysplasia, café-au-lait pigmentation, and autonomous hyperfunction of multiple endocrine system [1]. Growth hormone (GH) and/or prolactin (PRL) secreting pituitary adenomas associated with McCune-Albright syndrome have been reported [1–19]. However, only a few well documented cases on histology have been described [1,6].

We report here a patient with McCune-Albright syndrome who developed gigantism due to a histologically confirmed pituitary adenoma, and document the presence of GH and PRL in the surgically removed specimen by double immunostaining.

Case Report

A 11-year-old boy presented with right temporal hemianopsia January, 1998. He was referred by an ophthalmologist for evaluation of a possible pituitary adenoma. At the age of six, he underwent surgery for facial deformities due to fibrous dysplasia in an other hospital. He was blind on his left eye after the operation for fibrous dysplasia. At the time of admission the patient presented with acromegalic features. He was 170 cm tall, weighing 66 kg. The left side of his face was slightly deformed with bulging of the forehead and mandible. There was a café-au-lait spot on his right face. Basal level of serum GH and PRL were 103.6 ng/ml (normal <3 ng/ml) and 259.1 ng/ml (normal <30 ng/ml), respectively. Other endocrine functions were normal. Computed tomography showed hyperostosis of the right frontal, sphenoidal and maxillary bone (Fig. 1). Magnetic resonance imaging (MRI) revealed a pituitary macroadenoma with intraadenomatous cyst and marked decrease in signal intensity in the clivus (Fig. 2). On the basis of physical, endocrinologic and neuroradiologic examination, he was diagnosed as pituitary adenoma with McCune-Albright syndrome.

Surgical intervention was performed by subfrontal approach because of the small sella turcica with massive increase in thickness of the sphenoidal and maxillary bones. Puncture of the intraadenomatous cyst and partial removal of the macroadenoma were performed.

Pituitary tissue obtained at surgery was immediately fixed in 10% formalin and embedded in paraffin. Sections of 5 μm were stained with hematoxylin & eosin (H&E). Immunostains were performed for adenohypophysial hormones using the avidin-biotin-peroxidase

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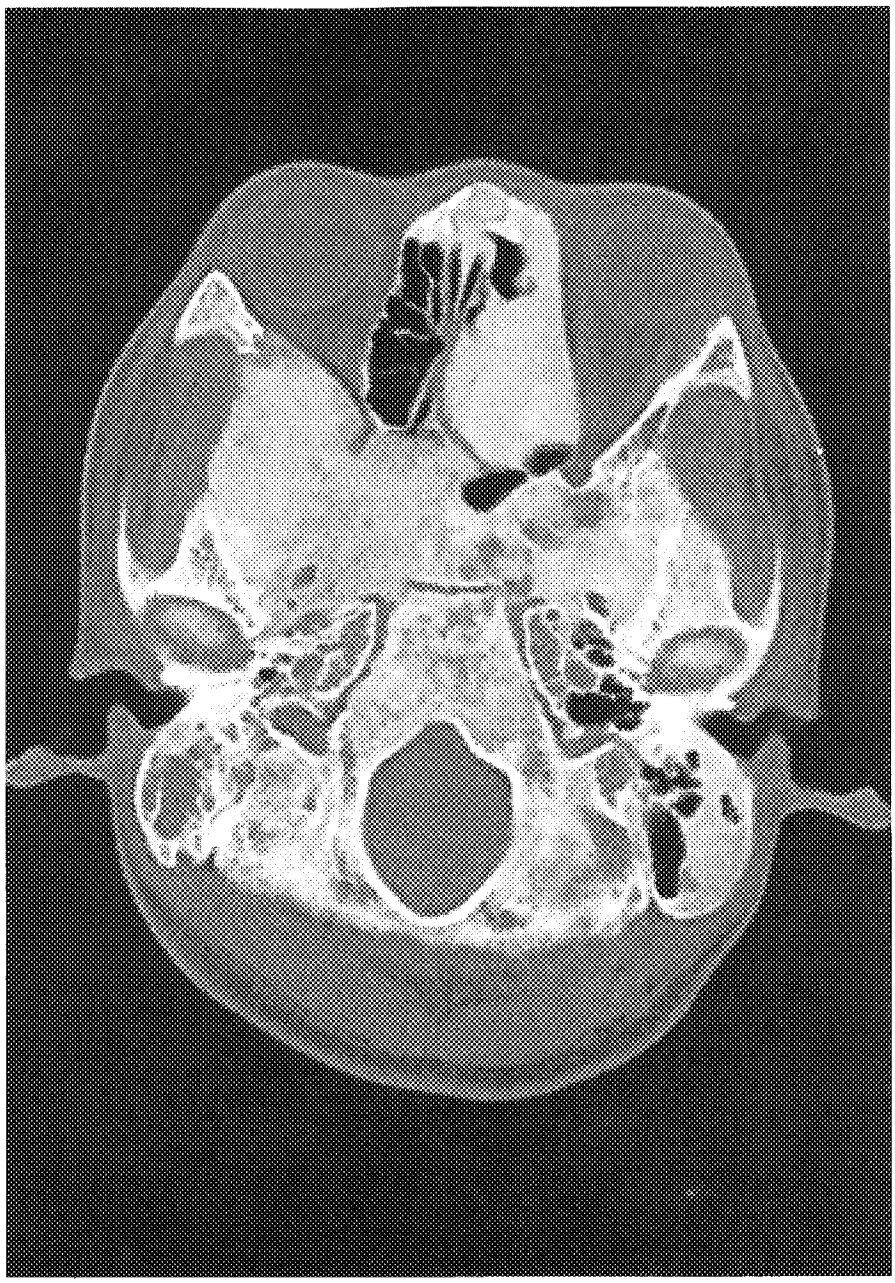

Fig. 1. CT scan demonstrating hyperostotic formation of the right frontal, sphenoidal and maxillary bone.

complex (ABC) method. For double immunostaining, sections were incubated with anti-PRL antibody, biotinylated IgG, and avidine-biotinylated peroxidase complex. Peroxidase activity was visualized with 3,3'-diaminobenzidine. After washing with PBS, the sections were incubated with anti-GH antibody, biotinylated IgG, and avidine-biotinylated alkaline phosphatase complex. Alkaline phosphatase activity was visualized by alkaline phosphatase substrate.

By light microscopy with H&E staining, the tumor represented a typical acidophilic adenoma of the pituitary (Fig. 3). The ABC method revealed immunoreactivity for GH and/or PRL in most of the adenoma cells. Immunostains were negative for ACTH, TSH, and FSH. Very small number of cells were positive for LH. Double immunostaining for GH and PRL demonstrated the co-existence of the two hormones in a few adenoma cells, the majority of the adenoma cells expressed either GH or PRL only (Fig. 4). Tissue obtained from the right sphenoidal bone was stained with

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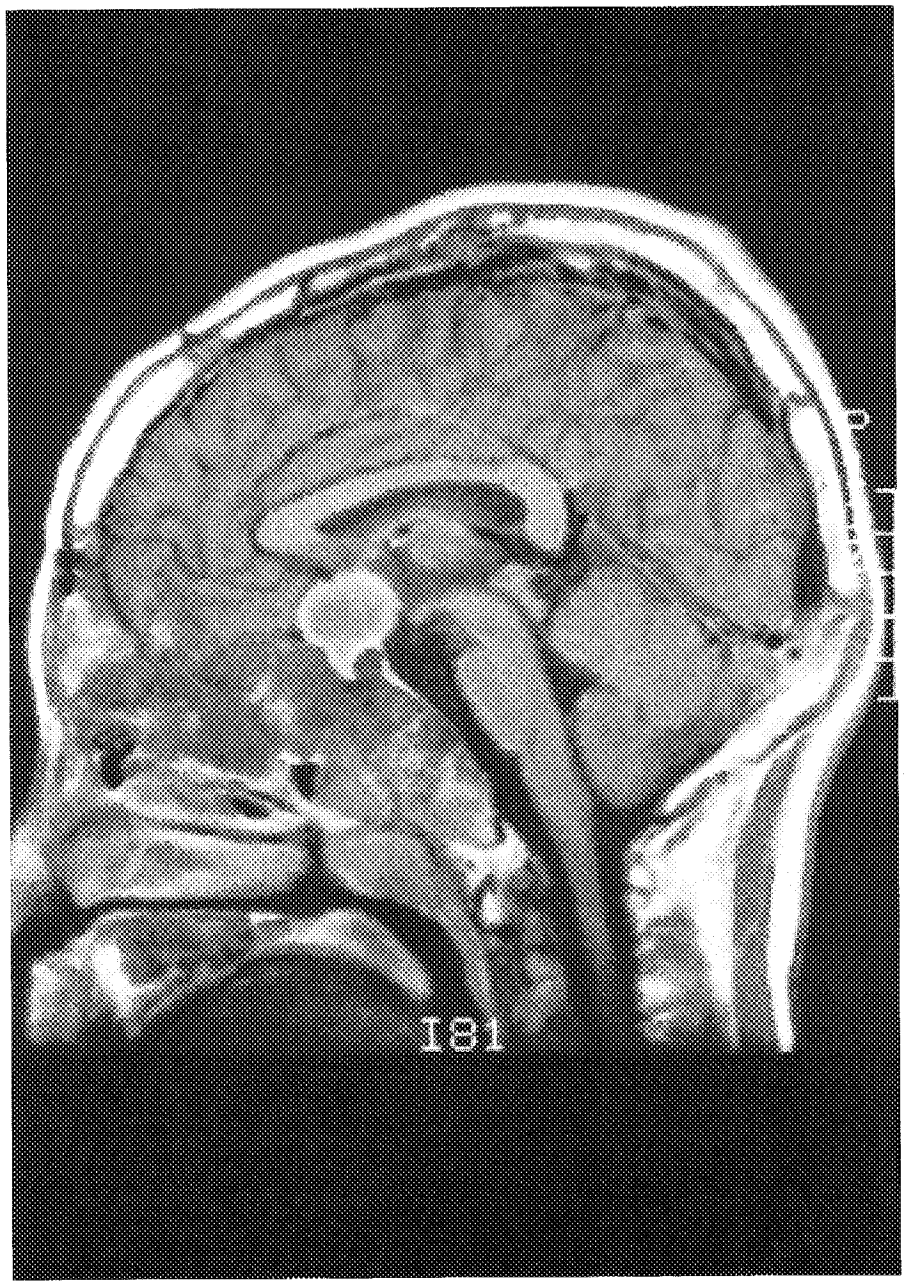

Fig. 2. *MRI showing a pituitary macroadenoma with intraadenomatous cyst and marked decrease in signal intensity in the clivus.*

H&E. Light microscopy revealed that the tissue composed of irregular trabecula of coarse woven bone and fibrous tissue. The borders of the bones merged with the surrounding cells without a conspicuous rim of osteoblasts. These findings were consistent with the diagnosis of fibrous dysplasia.

After surgery, the right temporal hemianopsia improved. Postoperative endocrinologic examination revealed reduction of basal serum GH and PRL levels. Administration of bromocriptine induced substantial decrease of serum PRL, but had very little effect on GH hypersecretion.

Discussion

Although more than 30 cases of acromegaly in association with the McCune-Albright syndrome have been reported, histologic studies were made in only 8 cases including our case (Table 1). Immunohistochemistry

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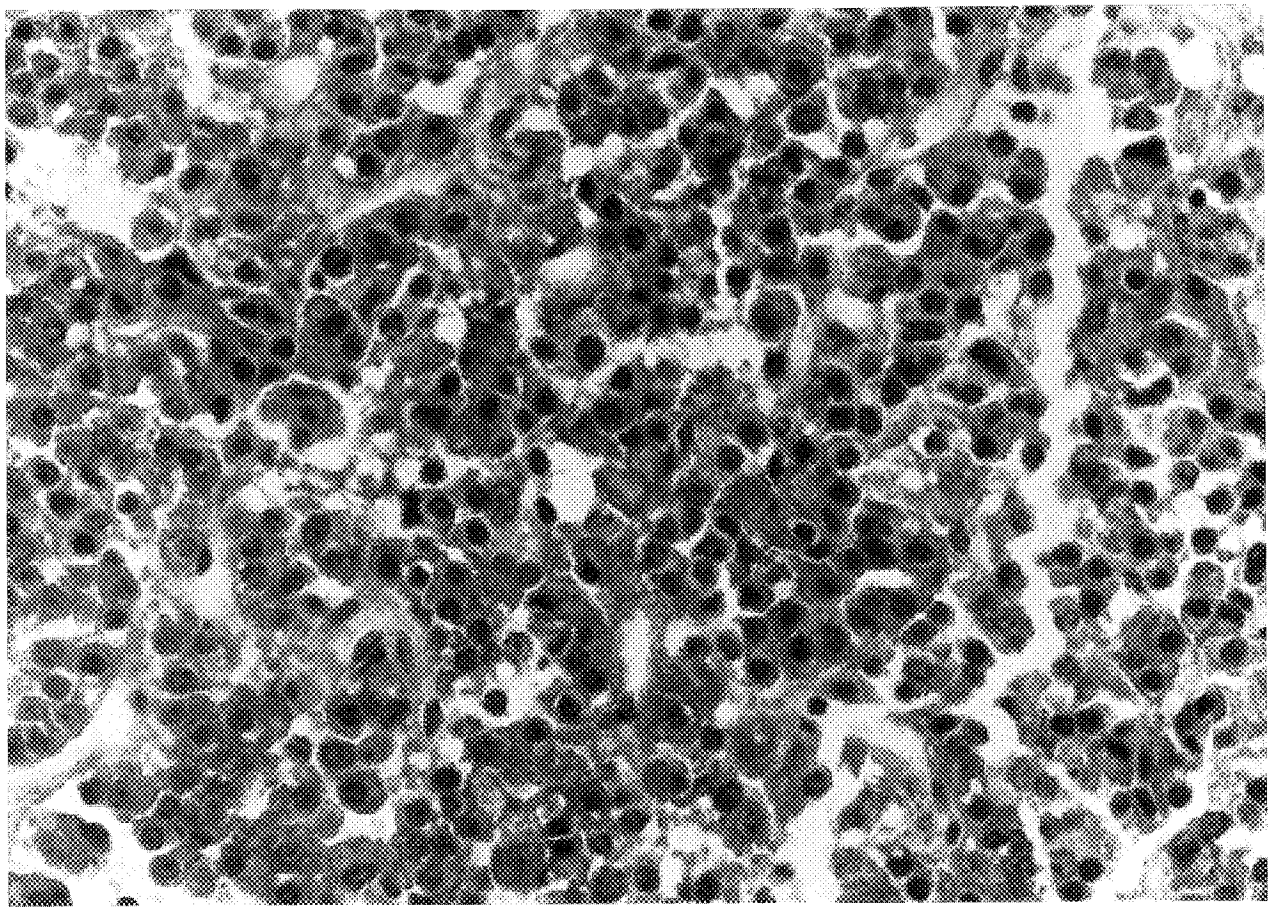

Fig. 3. Histology reveals a typical acidophilic adenoma of the pituitary (H&E ×480).

was performed in 6 cases, however, immunohistochemical localization of pituitary hormones have not been sufficiently examined. Kovacs et al. reported a case of mammosomatotroph hyperplasia associated with acromegaly and hyperprolactinemia in a patient with the McCune-Albright syndrome [6]. They demonstrated immunoreactivity for GH and PRL in the same area using consecutive sections. In this case report, we demonstrate immunohistochemical localization of GH and PRL using double immunostaining. The majority of adenoma cells expressed either GH or PRL. Although we do not study the pituitary adenoma by electron microscopy, the immunohistochemical results suggest that this adenoma might be a mixed GH-PRL cell adenoma [20].

Hyperprolactinemia is frequently encountered (71%) in acromegalic patients with McCune-Albright syndrome [13]. In contrast, hyperprolactinemia is found in 30–40% of patients with acromegaly unrelated to the McCune-Albright syndrome [15]. The high incidence of hyperprolactinemia and GH hypersecretion may be due to the frequent occurrence of bimorphous or plurimorphous tumors in McCune-Albright syndrome similar to our case. The cytogenesis of pituitary adenomas consisting of two different cell populations is not clear and remains to be elucidated [21].

In most cases of McCune-Albright syndrome, acromegaly is diagnosed on the basis of growth acceleration rather than on facial dysmorphism since the latter is usually masked by fibrous dysplasia [17]. The pituitary lesion is difficult to access, owing to unavailability of reliable imaging methods in earlier reports. MRI made it possible to demonstrate the pituitary lesion clearly, and the well documented cases of pituitary adenomas associated with McCune-Albright syndrome have been reported [10,17].

Surgery is the treatment of choice, but it is hazardous due to the high vascularity of the bone adjacent to the pituitary [13]. Fractionated radiotherapy should be avoided because it may lead to the development of post-irradiation sarcoma [11]. This problem may be resolved by stereotactic radiosurgery which allows a reduction in the radiation dose applied to the area surrounding the target. The usefulness of stereotactic ra-

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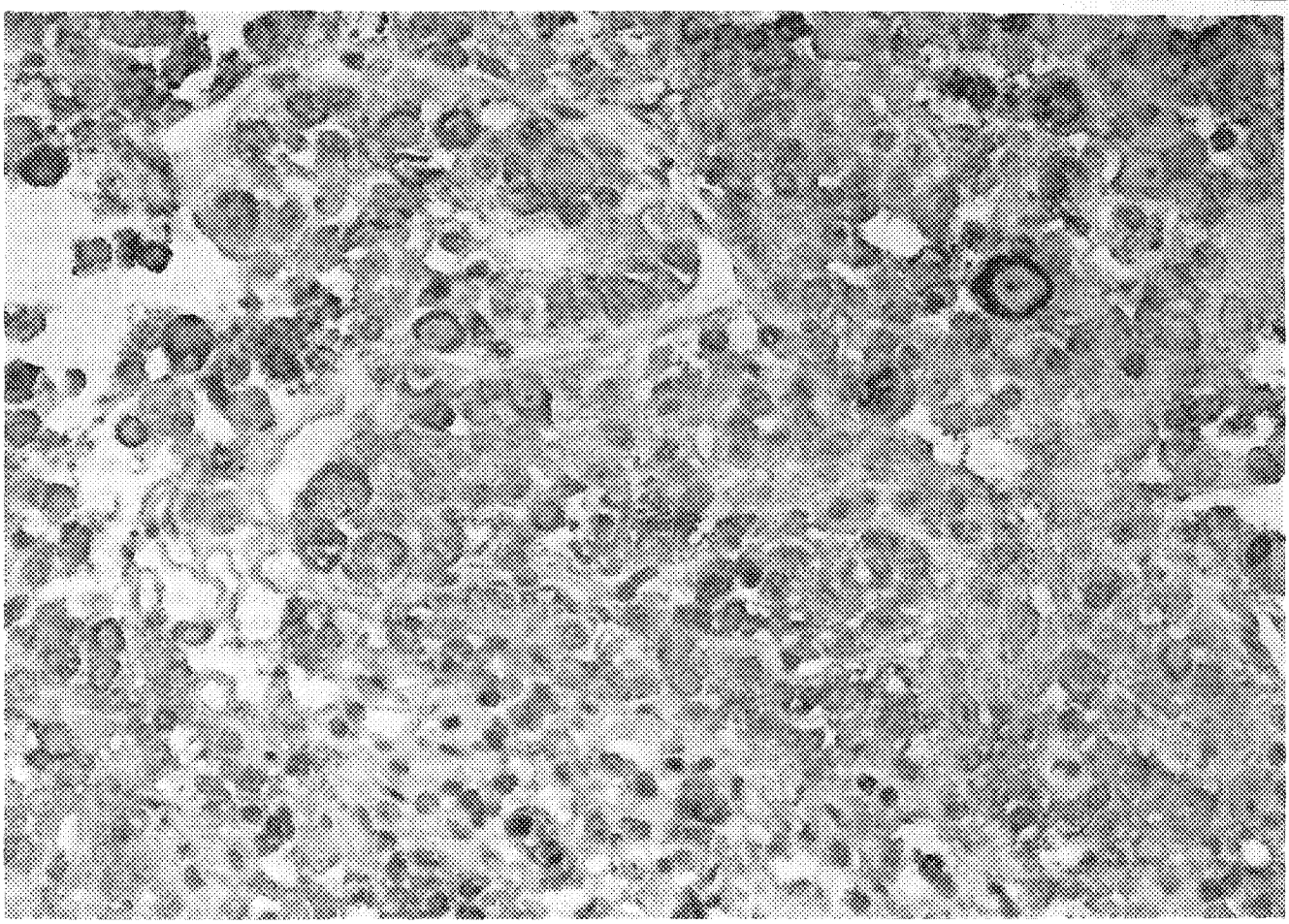

Fig. 4. *Double immunostaining for GH and PRL demonstrates that the adenoma cells expressed either GH or PRL only. The reaction products of red and brown indicate GH and PRL respectively (×480).*

diosurgery for recurrent acromegaly resulting from unsuccessfully resected tumors has been emphasized [22]. In our case, administration of bromocriptine induced marked decrease of serum PRL level. However, it had a limitted action upon GH hypersecretion. The therapeutic response to octreotide offers more promise. Reduction of GH hypersecretion and a shrinkage of pituitary macroadenoma was reported in a patient

Table 1. *Histologically confirmed cases of pituitary adenoma associated with McCune-Albright syndrome*

Case	Age	Sex	HE	Positive immunostaining	EM	Elevated serum hormone	References
1	29	M	chromophobic and focal acidophilic	GH, PRL, TSH	ND	GH, PRL, T3, T4, TSH	[1]
2	11	F	acidophilic	GH, PRL	done	GH, PRL	[6]
3	17	M	chromophobic	ND	ND	GH	[7]
4	25	F	chromophobic	ND	ND	GH, PRL	[10]
5	26	F	acidophilic	GH	ND	GH	[17]
6	47	F	acidophilic	GH	ND	GH	[18]
7	6	M	unknown	GH, PRL	ND	GH, PRL	[19]
8	11	M	acidophilic	GH, PRL	ND	GH, PRL	present case

ND: not ditermined; EM: electron mictoscopic study; GH: growth hormone; PRL: prolactin.

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with pituitary adenoma associated with McCune-Albright syndrome [9]. We suggest that the combination of a octreotide and stereotactic radiosurgery may be the treatment of choice in patients with pituitary adenoma and McCune-Albright syndrome.

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